

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

NATIONAL INSTITUTES OF HEALTH

TO : CTR members Drs. Hockett, Kreisher,
Sommers, Gardner

DATE: June 8, 1973

FROM : Dr. Robert Huebner *ryd*

SUBJECT: Site Visit to Dr. Severi's Laboratory at the Division of Cancer Research,
University of Perugia, Perugia, Italy.

I drove a rental car from Rome to Perugia on May 28, 1973 for a meeting with Severi's group on May 29; I drove back to Rome on May 30. My expenses were \$150.00.

In attendance at the meeting were Drs. Severi, Biancifiori, Bolis, Bucciarelli and Ribacchi.

The work on the CTR grant concerned with sheep lung adenomatosis (carcinoma?) is being carried on primarily by Ribacchi and Bucciarelli. This seemed quite appropriate since these two younger investigators are very much "with it" concerning recent work and literature concerning the role of RNA tumor viruses as likely causes of leukemia and cancer and they are particularly familiar with recent observations and publications by Scottish (Edinburgh) and Israeli workers which suggest that RNA tumor viruses are involved in the etiology of this lung cancer disease. The virus resembles type C and is distinct from visna virus, another RNA virus of sheep which is different in its pathogenic, biochemical and morphological properties.

During the period of the grant, Ribacchi and Bucciarelli succeeded in establishing and propagating for 22 subcultures a transformed "tumor" cell line from ovine adenomatosis lung tissue obtained from the University of Edinburgh (see pictures enclosed). Unfortunately, the line was lost at 23rd subculture. Extensive attempts to obtain fresh lung tumors from local abattoirs in Umbria have been fruitless. It appears now that the best sources available are Scotland and Sardinia. In order to get worthwhile specimens, Ribacchi feels that it is necessary for him to actually go and collect them personally. I agree with this assessment. His one successful cell culture was derived from the only tumor so far made available and all future efforts in his laboratory depend upon the feasibility of obtaining sufficient tumors from the field. This will require funds earmarked for this purpose which apparently are not currently available. I suggested therefore that they approach this supply problem forthrightly in their new proposal.

When I suggested that the original tumors and the cultures derived from them should have been tested regularly for the RNA dependent DNA polymerase as a sensitive indicator of virus, Ribacchi replied that they realized this

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but did not have the biochemical expertise available. They are, however, arranging now for such tests with the Department of Biochemistry at the University of Perugia. In reply to my question about the availability of the necessary equipment (collectors and counters) to do the test, Ribacchi stated that he was exploring this and would include such information in the proposal. I pointed out that at any point at which they succeeded in demonstrating RDP or type C viruses in tumor cell cultures, I could arrange through our NCI program to have such results confirmed and carried toward a more specific diagnosis.

In summary, Ribacchi and Bucciarelli have been working to establish in vitro cultures of ovine lung carcinoma. They have had a measure of success (see prints); they are knowledgeable concerning the state of the art and are eager to develop a laboratory test system for isolating the virus observed in lung tumors and cell cultures in Israel. From their work with the BALB/c mouse system, I feel they have a reasonably good prospect for doing this provided the tumor tissues are made available in good condition and in sufficient amounts to permit identification of viruses being observed by electron microscopy (Bucciarelli). Such materials would be useful for studies of the effects of the putative lung tumor virus in experimental animals.

Since there are no limitations against importation of such material into Italy where the disease is already endemic and since Ribacchi has made contacts in Edinburgh and plans to do likewise in Sardinia, the only limitations appear to be travel funds for acquisition of suitable materials. Materials sent by mail have proven worthless.

Perhaps it would be desirable for John Kreisher or some other Council Staff person to be assigned to help with acquisition of suitable supplies from areas known to have frequent lung adenomatosis. Unfortunately, nothing can be done about this problem in the U.S. since such materials would not be allowed to enter here. Inoculation of sheep lung tumor cells into lungs of BALB/c mice resulted in transfer in a number of unexpected tumors, but not lung tumors. I suggested that they study these tumors for virus which might be different from the mouse viruses.

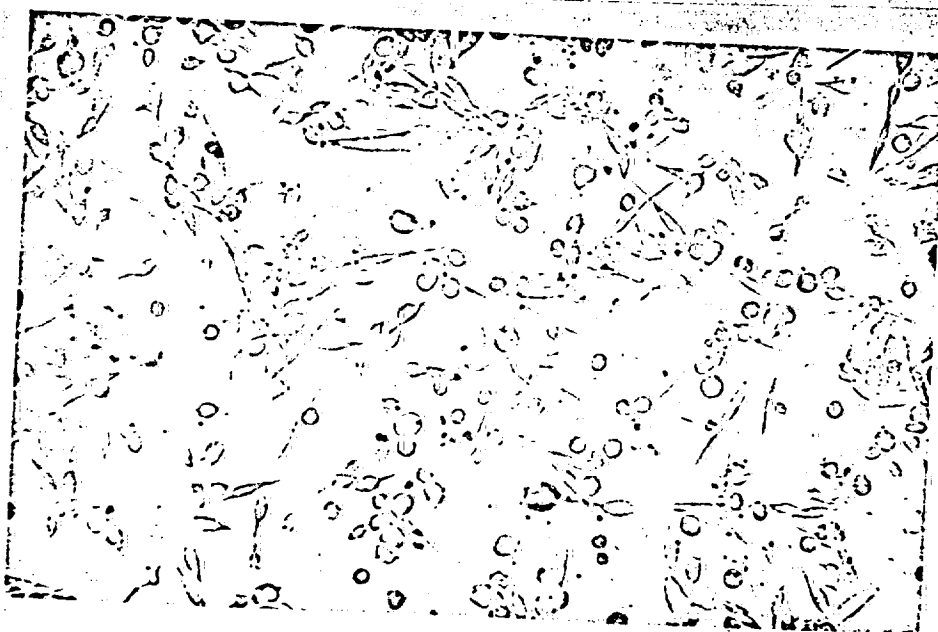
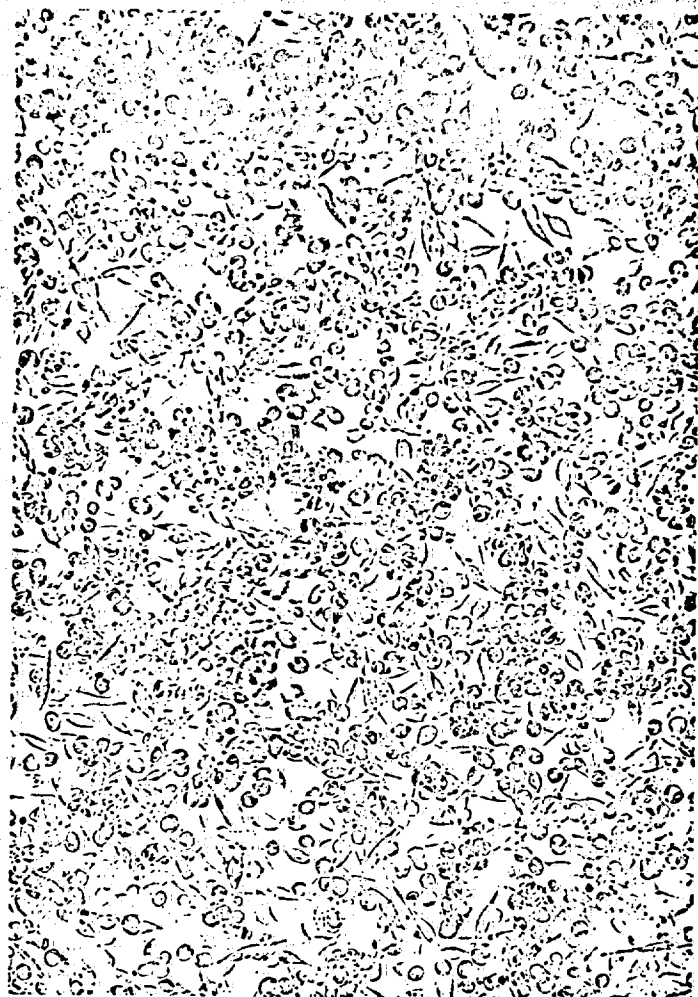
Of the two or three groups now working on this problem, I believe that Ribacchi and Bucciarelli have as good a chance as any to establish the necessary cultures and to identify and culture the type C RNA virus already seen in the tumors by electron microscopy. Once isolated the virus could also then be worked with in other laboratories and compared with other slow sheep viruses such as visna. The availability of a specific lung cancer-inducing virus would prove to be very interesting not only to the Council but also the entire research community concerned with the etiology of cancer.

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I have promised to send Ribacchi diagnostic antiserum capable of detecting the interspecies specific (gs-3) antigen of the mammalian RNA tumor viruses. He will need this to identify the virus when present in lung tumors (tissues and cultures).* We will also supply specific antisera to gs-1 of the mouse tumor viruses so that Ribacchi, Bucciarelli and Biancifiori can wrap up their previous CTR-supported studies of type C virus in BALB/c lung tumors.

* S. Shiflett: Should this be goat antigen to FeLV virus? Call Gilden for best materials.

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